

EVALUATION OF RADICAL CHOLECYSTECTOMY FOR INCIDENTAL GALLBLADDER CARCINOMA DIAGNOSED AFTER CHOLECYSTECTOMY, SINGLE CENTER EXPERIENCE

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ABSTRACT

Objective: To evaluate the procedure of radical cholecystectomy for incidental gallbladder carcinoma diagnosed after cholecystectomy at a tertiary care teaching hospital of Pakistan.

Study Design: Observational study (case series).

Place and Duration of Study: Army Liver Transplant Unit, Pak Emirates Military Hospital, Rawalpindi, from Jun 2018 to Apr 2019.

Methodology: A prospective study was conducted on 11 patients who underwent routine cholecystectomy either open or laparoscopic for a possibly benign condition but were found with a malignancy on histopathology, were included in the study. Detailed assessment regarding all the side effects was done immediately after the procedure, at 48 hours, at time of discharge and two weeks after the procedure was done on all the participants.

Results: Out of 11 patients included in the final analysis, 06 were male and 05 were female. Mean age of patients put who underwent cholecystectomy and had incidental finding of cancer was 44.23 ± 3.621 . Mean duration of hospital stay after the surgery was 5.13 ± 2.175 . Most of the patients had well differentiated tumor. Post-operative pain was the commonest complication among the target population followed by biliary complication.

Conclusion: Gallbladder carcinoma may be missed on routine clinical screening and radiological modalities. Surgeon should be careful enough and suspect unusual finding of malignancy in routine surgeries. Radical surgery of the incidental gallbladder cancer emerged as an effective management modality among the patients managed in our set up during this study period.

Keywords: Cholecystectomy, Gall bladder carcinoma, Incidental.

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INTRODUCTION

Cholecystectomy is one of the most common abdominal surgeries performed in all parts of the world¹. Various methods have been used in the past, laparoscopic cholecystectomy is the method of choice in centers where expertise and equipment is not a problem². Usually this procedure has been performed for the benign diseases of the gall bladder or related structures but occasionally malignancies of the region also demand this procedure to be done on the patients³. In most of the cases prior diagnosis has been established with the less invasive diagnostic modalities and surgeon is well prepared regarding the nature of disease which he will find preoperatively but in some cases it is the incidental finding that the gall

bladder they were considering benign is actually neoplastic⁴. The proportion of these cases is usually high in developing countries with less diagnostic facilities at the periphery and high number of referrals⁵.

GI malignancies have been a common diagnosis in all parts of the world⁶. Gall bladder cancers have usually not been reported that frequently as other tumors of this region in the past. In recent times there is a rise in the incidence of the neoplasias of gall bladder and surgical oncologist need to have a knowledge and training of these cancers and their effective treatment⁷. Early recognition and treatment have been associated with good outcome and longer survival among these patients in various studies done in the past⁸.

A study done in our neighboring country India concluded that gall bladder carcinoma has been found notorious to deceive the radiologist

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and his modalities and first time caught either by the surgeon preoperatively or by the histopathologist on routine examination⁹. A meta-analysis done on the studies revolving around same subject concluded that laparoscopic cholecystectomy should not be withheld for patients of gall bladder cancer, rather its treatment of choice for the early cancers. Bile duct perforation was the commonest complication among these patients undergoing this procedure¹⁰. Another similar study done in Korea also strengthened the previously existing data that cholecystectomy has usually been sufficient for early tumors and second radical surgery may be planned in advanced cases or in those where free margins are needed to be achieved¹¹.

Despite its good safety profile multiple side effects have been observed in various studies in this procedure as well. Some of them include pain, wound discharge, hematoma formation, bile duct perforation^{12,13}. There can be few other rare complications also but essence lies in the awareness of surgeon and good communication to the patient prior to the management.

Being from a developing nation with limited resources this topic is of utmost relevance in good surgical practice. Very limited local data is available on this aspect and that too from private hospitals from another province^{14,15}, but no study has so far been conducted at a tertiary care military hospital receiving patients from all over Pakistan including the public sector tertiary care hospitals. This study was planned with the rationale to evaluate the procedure of radical cholecystectomy for incidental gallbladder carcinoma diagnosed after cholecystectomy at a tertiary care teaching hospital of Pakistan.

METHODOLOGY

This observational (case series) study was conducted at Army Liver Transplant Unit, Pak Emirates Military Hospital Rawalpindi from June 2018 to April 2019. Sample size was calculated by WHO Sample Size Calculator by using study of Khantan *et al.* With reference percentage as 10%⁸. Non probability Consecutive sampling technique

was used to gather the data. All patients between the age of 18 and 65 years who underwent routine cholecystectomy either open or laparoscopic for a possibly benign condition but were found with a malignancy were included in the study. Patients who were referred from other military, public sector and private hospitals who underwent cholecystectomy and were found with a neoplastic gallbladder were also included in the analysis in addition to the patients of own hospital. Exclusion criteria were the patients with less than eighteen year of age or those with uncontrolled diabetes or hypertension or any other physical illness. Those with a benign disease or ambiguous diagnosis were also not included. Patients with a known gallbladder carcinoma or any other solid or hematological malignancy were also made part of the exclusion criteria.

After ethics approval from the ethical review board committee (IRB letter A/28) and written informed consent from potential participants or their relatives, patients who had incidental finding of gall bladder carcinoma while undergoing routine cholecystectomy either open or laparoscopic at referring hospital fulfilling the above mentioned inclusion and exclusion criteria were included in the study. Routine analgesia and antibiotic cover was given to each patient as per the hospital protocol and condition of the patient. Gall bladder is sent to the histopathology department as per protocol of the unit. Gallbladders with suspicious gross appearance or other unusual findings were especially sent on priority with detailed notes of the surgeon. Two consultant histopathologists confirmed the report before the patient was labeled as cancer and enrolled in the study. VAS score was applied to assess the post-operative pain. Visual analogue score (VAS score) of greater than 6 was considered as significant pain. Cancer was staged according to the International Union against Cancer (Union for International Cancer Control) tumor node metastasis (TNM) staging system. Detailed assessment regarding all the side effects was done immediately after the procedure at 48 hours, at time of discharge and two weeks after the procedure was

done on all the participants. A special performa was designed for this study including the socio demographic profile and all the possible side effects of the procedure.

All statistical analysis was performed by using the Statistics Package for Social Sciences version 24 (SPSS-24). Frequency and percentages for gender, number of patients with incidental findings of cancer, and all the complications recorded during the study were calculated. Mean and standard deviation for age, stay at hospital and duration of symptoms before the surgery was also calculated for the study participants.

RESULTS

A total of 16 patients were initially approached to get them included in the analysis. Two had diagnosis of cancer before the surgery while three had metastatic illness. Out of 11 patients included in the final analysis 06 (54.5%) were male and 05 (45.5%) were female. Mean age of patients put who underwent cholecystectomy and had incidental finding of cancer was 44.23 ± 3.621 years. Male to female ratio was 1:0.8. Mean duration of hospital stay after the surgery was 5.13 ± 2.175 days. Most of the patients had well differentiated tumor. Other characteristics of study population have been summarized in table-I. Post-operative pain was the commonest complication among the target population followed by bile duct perforation (table-II). Out of 11 patients, 04 (36.3%) had pT1a disease, 02 (18.2%) had pT1b, and 03 (27.2%) had T2 disease while only two had advanced disease which was diagnosed incidentally at the time of surgery (table-I).

DISCUSSION

Hepato-biliary surgery has been emerging as a promising specialty in last few years with a lot of modern modalities and advancement in surgical techniques¹⁶. Gallbladder is one of the most commonly removed organs via surgery in case of presence of pathology. Usual pathologies involving this organ are benign and resolved once it has been removed, still malignancies involving this are on a rise and surgeons need to be equipped with adequate expertise and staff in order

to manage the cancers of hepatobiliary region⁷. In west usually this task is achieved by the surgical oncologist but this specialty is still under developed in our part of the world. This prospective

Table-I: Characteristics of study participants (n=11).

Age (years)	
Mean \pm SD	44.23 \pm 3.621
Range (min-max)	19 - 62 years
Gender	
Male	06 (54.5%)
Female	05 (45.5%)
Duration of symptoms before surgery	55.44 \pm 6.145 days 9 days - 15 months
Mean duration of hospital stay	5.13 \pm 2.175 days
Stage of Tumor	
pT1a	04 (36.3%)
pT1b	02 (18.2%)
PT2	03 (27.3%)
Advanced	02 (18.2%)
Differentiation Status on Histopathology	
Well differentiated	08 (72.7%)
Moderately differentiated	03 (27.3%)

Table-II: Complications faced by the patients after the procedures of open or laparoscopic cholecystectomy in the study (n=11).

Medical Conditions	n (%)
Post-operative pain	06 (54.5%)
Bile duct perforation	03 (27.3%)
Shock	01 (9.1%)
Wound discharge	02 (18.2%)
Sepsis	01 (9.1%)
Others	01 (9.1%)

Table-III: Short term outcome of patients put underwent cholecystectomy and had incidental finding of carcinoma.

Total	No Complication	One Complication	More Than One Complication
11	03 (27.2%)	07 (63.6%)	04 (36.3%)

study was planned with the aim to look for the patients with incidental finding of cancer upon the surgery or at the routine histopathology at surgical unit of our hospital.

Only 11 patients were found eligible for our analysis in 10 months' time period. Similar results have been reported in the past as well as this is not a very common site for the primary tumor⁹. Though a small number, but still it reflects that there is a gap between exact diagnosis before the surgical management and incidental finding on

the table or at the time of routine histopathology. This highlights the fact that despite advancement in radio-diagnostic modalities and non-invasive techniques of investigating a disease, cancer of gallbladder is still escapable from these modalities and present as an incidental finding. A surgeon with adequate knowledge of this can have a strict eye on gross appearance of gallbladder at the time of surgery and can warrant the pathologist in advance as well.

Radical cholecystectomy in these patients did not produce more than expected number of complications. Mean stay of hospital was only slightly raised among these patients as compared to the mean hospital stay in benign gallbladder surgeries reported in other studies done on patients without the neoplastic findings¹⁷. This finding highlights the positive role of radical cholecystectomy among these patients, at least on the short term basis. More studies on long term results can strengthen our results.

Post-operative pain was the commonest complication in our patients after the radical cholecystectomy. VAS score as applied to ascertain this finding. Similar results were reported in other studies done in the recent past^{12,17}. Bile duct perforation was the second most common complication in our study. It has been recognized as a serious complication of surgery of this area and has also been encountered among the patients operated for benign gallbladder disease. Previous studies have reported this finding as most common among the patients with incidental carcinoma of gallbladder. Reason might be unexpected difficult surgery due to presence of a malignant disease instead of a routine benign gallbladder.

Mean duration of clinical symptoms before the surgical intervention was around 55.44 ± 6.145 days in our target population. It is quite high as compared to the people who undergo surgery for benign problems^{17,18}. Reason of late presentation and choosing the option of surgical management after adequate time has passed may spread the disease and become predictor of poor prognosis. Even for benign gallbladder symp-

toms wax and wane for years sometimes before the patient opts for the definitive management. Therefore this parameter has usually no significant value in predicting the nature of disease among the patients undergoing surgery.

Most of the patients have well differentiated disease on the histopathology findings. Staging of tumor in these patients also revealed that most tumors were within the early stage. These findings have been reported in the past as well in the studies done on the patients with incidental gall bladder cancer¹⁹. Reason of this might be that early and well differentiated tumors are too small and also mimic normal tissue so have more chances of getting missed on the routine diagnostic protocols.

Strict exclusion criteria and including purely incidental cases has been the strength of this study but it has few limitations as well. Long terms follow up and five year survival was not made part of the study design which cannot justify it treatment of choice for the incidental gallbladder. Further, clinical and radiological parameters before the surgery were not compared to see the difference between benign and malignant disease before the incidental diagnosis. Difference in the outcome among the patients undergoing open and laparoscopic cholecystectomy was also not studied. Sample size was quite small as it is a low incidence disease and inclusion/exclusion criteria were strict as well. Future studies with a wide study time and long term follow up may throw more light on this subject.

CONCLUSION

Gallbladder carcinoma may be missed on routine clinical screening and radiological modalities. Surgeon should be careful enough and suspect unusual finding of malignancy in routine surgeries. Radical surgery of the incidental gallbladder cancer emerged as an effective management modality among the patients managed in our set up during this study period.

CONFLICT OF INTEREST

The study has no conflict of interest to declare by any author.

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